REMARKS

Entry of the claim amendments is respectfully requested. Claims 3, 8, 14, 17, 19, and 21 are pending. Independent claims 3 and 17 have been amended to incorporate the limitation in dependent claims 13 and 20 that the mammal be a ruminant. Claims 14 and 21 have been amended to properly depend from claims 3 and 17, respectively. No new matter has been added.

Claims 3, 8, and 13-15 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner contends that no basis or support is found in the present specification for the designation "DSX 6601" for an *E. coli* strain. Claims 13 and 15 have been cancelled, and claims 3, 8 and 14 clearly recite (and have always recited) the designation "DSM 6601." Reconsideration and withdrawal of this ground of rejection are therefore respectfully requested.

Claims 3, 8, 13-17, and 19-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 13, 15-16, and 20 have been cancelled. With regard to claim 3, the Examiner contends that claim 3 is vague and indefinite in the incorrect designation "DSX 6601." Claim 3, however, clearly recites (and has always recited) the designation "DSM 6601."

With regard to claims 3 and 17, the Examiner contends that claims 3 and 17 are vague and indefinite in that the "therapeutically effective amount" required to "prevent"

diarrhea or to "prevent" intestinal colonization in all subjects for all conditions is not set forth with sufficient particularity in the as-filed written description. The Examiner also contends that the time period of "preventing" is also unclear. Applicant respectfully traverses this rejection. According to MPEP § 2173.05(c), the phrase "effective amount" is not indefinite if those skilled in the art would be able to determine from the written description what an effective amount is. The current specification clearly discloses that the objective of the current invention is to prevent and treat diarrhea in ruminants using DSM 6601. As such, an "effective amount" is an amount of DSM 6601 that achieves these objectives. Determining the concentration of DSM 6601 necessary to achieve these clear endpoints is well within the skilled artisan's knowledge. Applicants' invention almost completely prevented the occurrence of diarrhea due to fungi colonization, as compared to animals not treated with DSM 6601. This prevention extended for much longer than the 10-13 days of treatment, in some instances up to almost 10 weeks following treatment. (*see* p. 9, lns. 11-13). As such, claims 3 and 17 are not indefinite.

With regard to claim 8, the Examiner contends that claim 8 is vague and indefinite in that the time period encompassed by "at least about 10 days" is unclear, even when read in light of the specification. Applicant respectfully traverses this rejection. The current specification clearly states that DSM 6601 was "independent of the weight and age of the animal and was administered orally, specifically for a duration of 10-13 days after birth." (*see* p. 9, lns. 14-15). Thus, the specification teaches that the animals can be treated beginning immediately after birth or sometime soon thereafter for a period of at least about 10 days. As such, claim 8 is not indefinite. Reconsideration and withdrawal of this ground of

rejection are therefore respectfully requested.

Claims 3, 8 17, and 19 are rejected under 35 U.S.C. § 102(b) as anticipated by *Hockertz* or *Lodinova-Zadnikova et al.* or under 35 U.S.C. § 102(a) as being anticipated by DE 196 37 936. The claims pertain to a method for treating and preventing diarrhea mediated by gastrointestinal colonizing fungi in ruminants by orally administering a therapeutically effective amount of *E. coli* strain DSM 6601. As the current specification makes clear, after all existing therapeutic options had been exhausted, the oral administration of a suspension of DSM 6601 almost completely prevented the occurrence of diarrhea in suckling calves due to gastroenteritis (*see* pg. 10, lns. 5-8).

With respect to *Hockertz*, the reference pertains to the immunomodulatory effect of DSM 6601 on intravenously induced *Listeria* monocytogenes or *Candida* infection. It is reported that pathogen counts found in the respective organs, namely the liver and spleen, may be ameliorated by a single previous *E. coli* challenge. In this mouse model system, *intravenously* administered *Listeria* and/or *Candida* induce a *systemic* inflammation.

Hockertz does not teach or suggest the use of DSM 6601 to treat or prevent diarrhea caused by fungi in the gastrointestinal tract of ruminants. In contrast to ruminants with multicompartmental stomachs, monogastric mammals like mice have a totally different gastrointestinal tract with respect to anatomy, physiology, biochemistry, microbiology, and infectology. As such, *Hockertz* cannot anticipate the claimed invention.

With respect to *Lodinova-Zadnikova et al.*, the reference pertains to the administration of DSM 6601 to newborn human babies to prevent or reduce colonization of the

gastrointestinal tract by pathogenic bacteria. The reference reports that prophylactic administration of DSM 6601 reduced pathogenic bacteria load.

Like *Hockertz*, *Lodinova-Zadnikova et al.* does not teach the use of *E. coli* to prevent or treat diarrhea caused by fungi in the gastrointestinal tract of ruminants. As such, *Lodinova-Zadnikova et al.* cannot anticipate the claimed invention.

With respect to DE 196 37 936, Applicant notes that it has made a claim for foreign priority benefits under 35 U.S.C. § 365 based on DE 197 51 907, filed November 22, 1997, which predates the April 9, 1998 publication date of DE 196 37 936. In this respect, Applicant hereby submits a certified English translation of priority document DE 197 51 907. As the current application and the priority document share identical specifications, DE 196 37 936 cannot anticipate the claimed invention.

Claims 3, 8, 13-17, and 19-21 are also rejected under 35 U.S.C. § 103(a) as being obvious over *Hockertz* taken with *Lodinova-Zadnikova et al.* and DE 196 37 936. Claims 13, 15-16, and 20 have been cancelled. Claims 3, 8, 14, 17, 19, and 21 provide methods for treating and preventing fungi-induced diarrhea in ruminants by the oral administration of *E. coli* strain DSM 6601.

As the current specification makes clear, after all existing therapeutic options had been exhausted, the oral administration of a suspension of DSM 6601 almost completely prevented the occurrence of diarrhea in suckling calves due to gastroenteritis (*see* pg. 10, lns. 5-8). Significantly, none of the documents cited teach the use of *E. coli* strain DSM 6601 to treat diarrhea caused by pathogenic fungi in ruminants, nor do they suggest such a treatment, either alone or in combination.

With respect to *Hockertz*, the skilled artisan has been taught to use a single orally given challenge of DSM 6601 to reduce an induced systemic infection of *Candida* or *Listeria monocytogenes* in the mouse. Significantly, this challenge is reported to ameliorate the pathogen count of infested organ such as the liver and spleen. *Hockertz* does not teach or suggest gastrointestinal infection by fungi resulting in diarrhea. Additionally, *Hockertz* does not teach or suggest diarrhea in ruminants having a completely different anatomical, physiological, biochemical, microbiological, and infectological interrelationships as compared to monogastric animals such as mice and humans. One of skill in the art would recognize that it is difficult or even impossible to compare systemic infection data from mice to fungi-mediated diarrhea in ruminants. Moreover, prior to Applicants' current invention, a single challenge of DSM 6601 has never been reported to cure diarrhea in any system. As such, *Hockertz* does not render the claimed invention obvious.

Nor does the combination of *Hockertz* with *Lodinova-Zadnikova et al.* render the claimed invention obvious. In *Lodinova-Zadnikova et al.*, the skilled artisan has been taught to use DSM 6601 to prevent or reduce infestation of the gastrointestinal tract in new-born human babies by pathogenic bacteria. Like *Hockertz*, *Lodinova-Zadnikova et al.* does not teach or suggest gastrointestinal infection by fungi resulting in diarrhea, nor does it teach or suggest diarrhea in ruminants. As such, the skilled artisan could not provide the material missing from Hockertz with any teaching or suggestion in *Lodinova-Zadnikova et al.* to arrive at the subject matter of the present invention. Accordingly, *Lodinova-Zadnikova et al.* does not, alone or combination, render the claimed invention obvious.

With regard to DE 196 37 936, as discussed above,

Applicant notes that it has made a claim for foreign priority benefits under 35 U.S.C. § 365 based on DE 197 51 907, filed November 22, 1997, which predates the April 9, 1998 publication date of DE 196 37 936. As such, DE 196 37 936 cannot, alone or in combination, be used to render the claimed invention obvious.

In view of the above remarks, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that she telephone Applicant's attorney at (908) 654-5000 in order to overcome any additional objections which she might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

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Respectfully submitted,

By /

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